



Brigham and Women's Hospital

Founding Member, Mass General Brigham

Metabolic Management of Kidney Stones

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Clinical focus: Nephrolithiasis

Research focus: Nephrolithiasis, CKD, Gout, Hearing Loss, Tinnitus, Shingles



DISCLOSURES

I have financial relationships or affiliations with:

<u>Name of Organization</u>	<u>Relationship</u>
UpToDate	Section Editor, Author
GSK	Grant Support
OM1	Equity
Atom Bioscience	Consultant



Kidney Stones Can Be Prevented

OBJECTIVES

Use case vignettes to:

- Review the presentation and evaluation of patients with different types of kidney stones
- Review the approaches to prevent stone recurrence



Case #1—Mr. M.T.

- 52 y.o. male with recurrent nephrolithiasis
- Passing small pieces, orange colored, “continuously
- PMH: ulcerative colitis, s/p colectomy
- Meds: finasteride, SSRI, vitamin D, acyclovir

Case #1—Evaluation

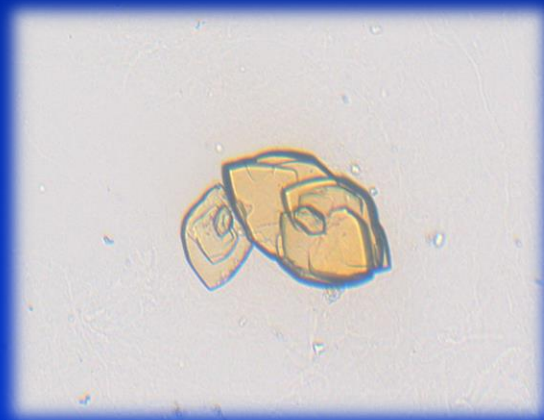
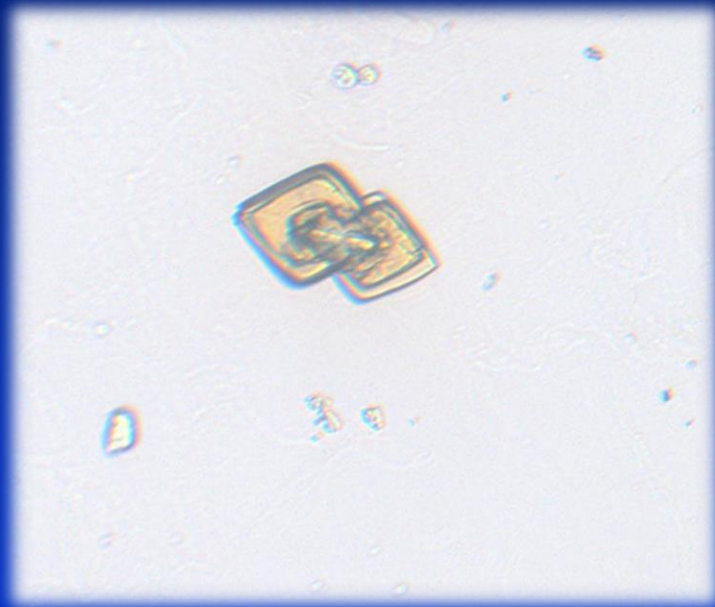
- Blood
 - Bicarbonate 28 meq/L
 - Creatinine 1.40 mg/dl
 - Calcium: 9.3 mg/dl
 - Uric acid: not measured
- No recent imaging

Renal Consult Requested

- Stone type?
- Evaluation?
- Treatment?

What Is the Most Likely Stone Type?

- A. Calcium oxalate
- B. Calcium phosphate
- C. Uric acid
- D. Cystine

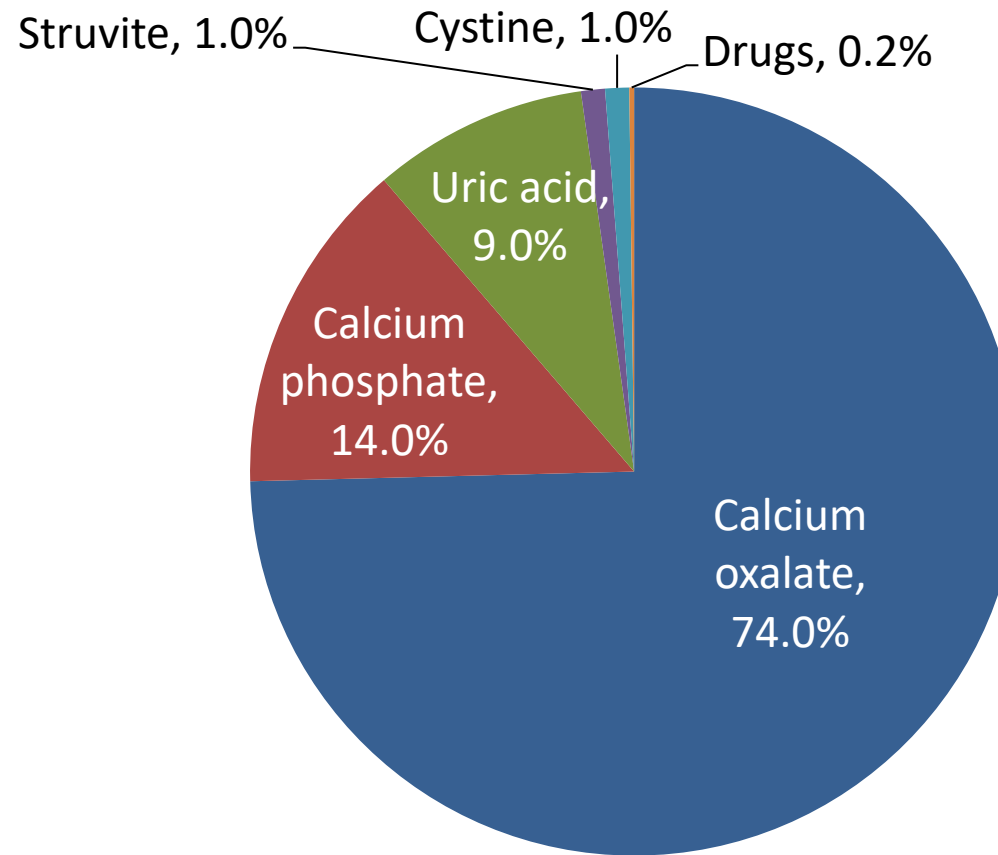


Answer: Uric Acid

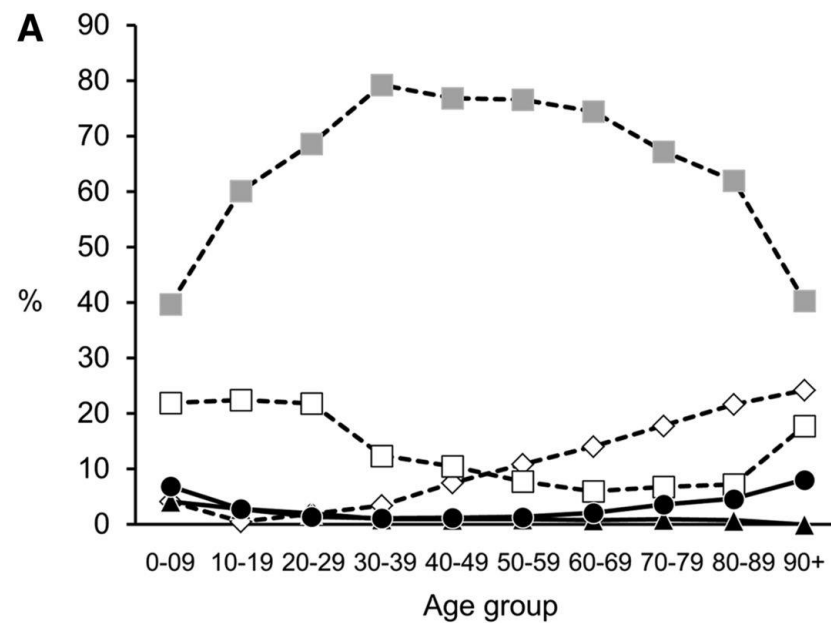
- Rapid stone formation
- Chronic GI losses → persistently acidic urine



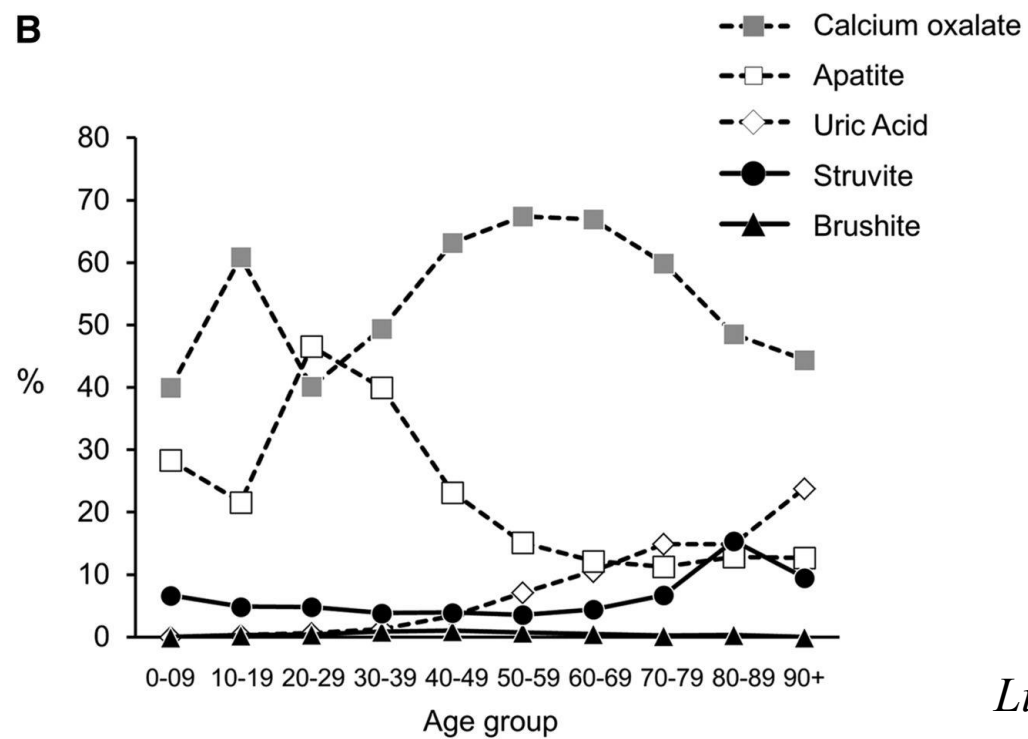
Types of Stones in First Time Stone Formers



Men



Women



Types of Stones and Causes

- **Calcium oxalate**—low urine volume, high calcium, high oxalate, low citrate
- **Calcium phosphate**—low urine volume, alkaline urine, high calcium, low citrate, high phosphate
- **Uric acid**—persistently acid urine, high urine uric acid
- **Cystine**—autosomal recessive disorder
- **Struvite**—urease producing bacteria in upper tract

Case #1—Mr. M.T.

- 52 y.o. male with recurrent nephrolithiasis
- Passing small pieces in urine, orange colored, “continuously”
- PMH: ulcerative colitis, s/p colectomy
- Meds: finasteride, SSRI, vitamin D, acyclovir

Case #1—24-hour urine results

<u>TV</u>	<u>Ca</u>	<u>Ox</u>	<u>Cit</u>	<u>UA</u>	<u>Creat</u>	<u>Na</u>	<u>pH</u>
2.4	290	56	141	503	2599	347	5.6
1.5	172	20	142	231	1528	237	5.3

Question: Metabolic abnormalities?

Which urine is the correct one?

<u>TV</u>	<u>Ca</u>	<u>Ox</u>	<u>Cit</u>	<u>UA</u>	<u>Creat</u>	<u>Na</u>	<u>pH</u>
2.4	290	56	141	503	2599	347	5.6
1.5	172	20	142	231	1528	237	5.3

Question: Metabolic abnormalities?

Assume first urine is the correct one.

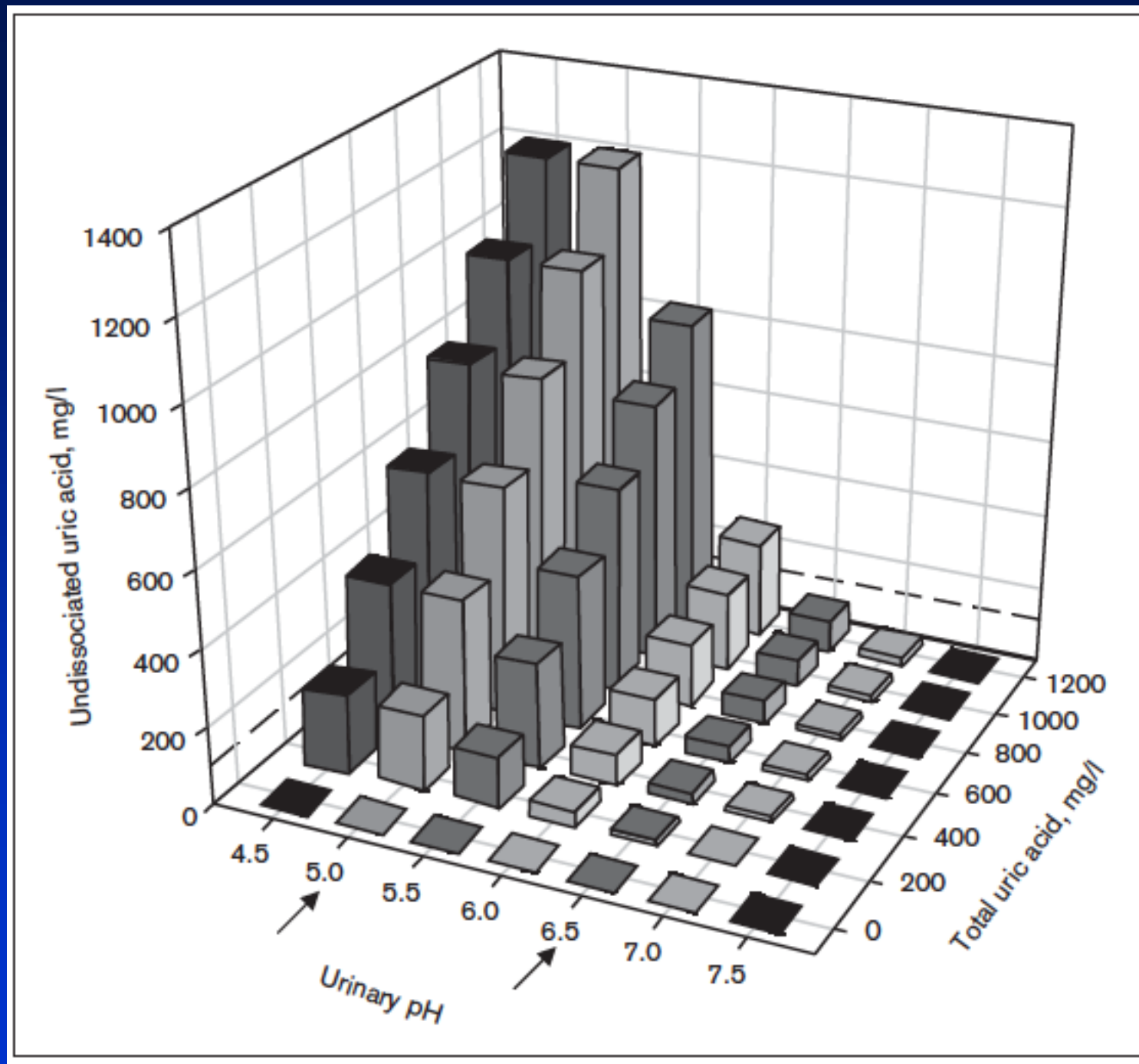
- High calcium, oxalate, sodium
- Low citrate
- Normal uric acid

Assume second urine is the correct one.

- High, sodium
- Low citrate
- Normal calcium, oxalate, uric acid

Question: Next Steps?

- Imaging study: Spiral CT (non-contrast)
- Repeat 24-hour urine
- Alkalinization of urine—**urine pH** is the most important risk factor for uric acid stones
 - Potassium citrate or bicarbonate (40-80 meq/d)
 - Patient checks urine pH (aim for ~6.5 or higher)



Case #2—Ms. G.K.

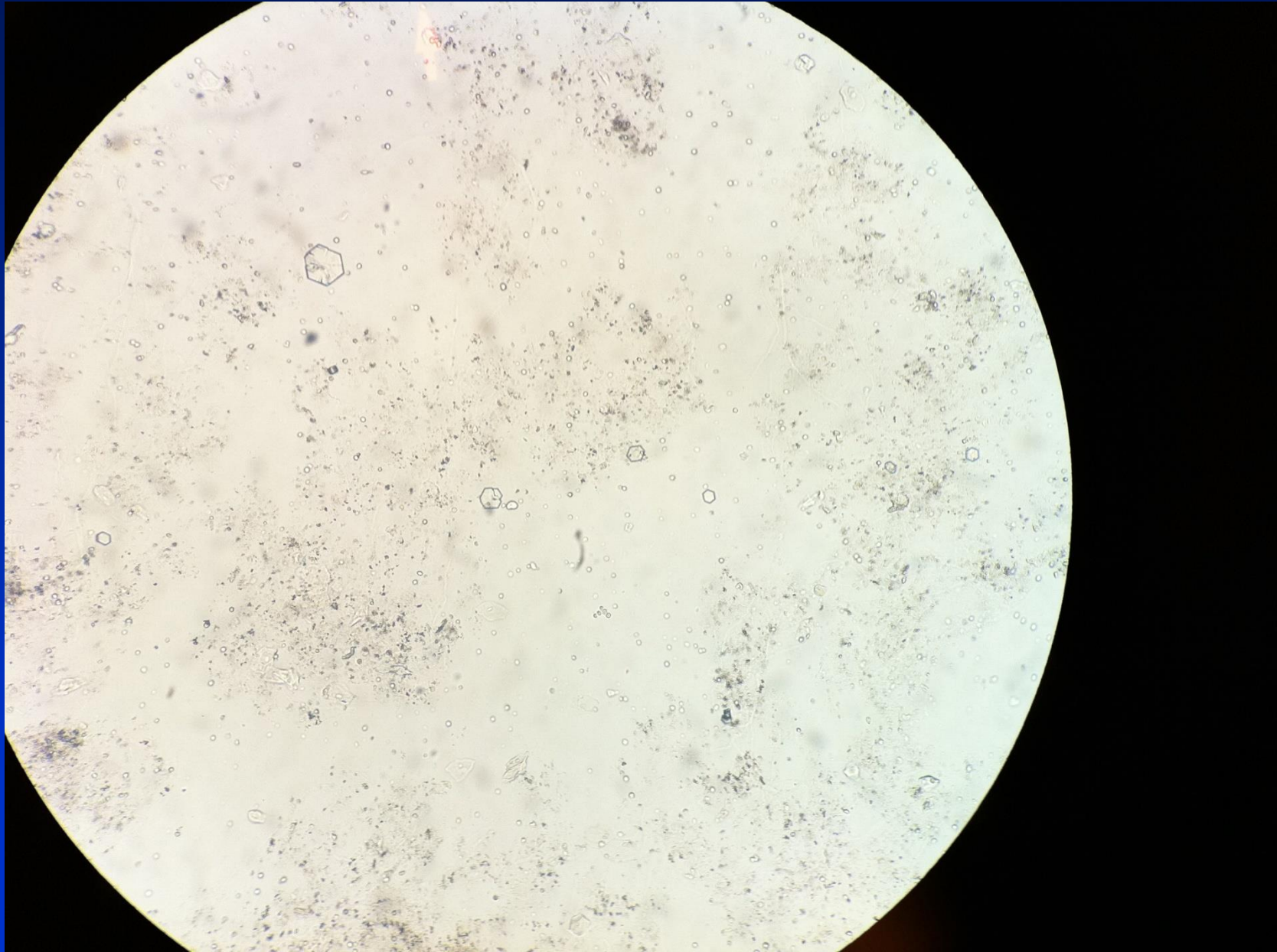
- 45 y.o. female with recurrent nephrolithiasis
- Frequency: every 8-10 months
- Previous procedures:
 - ESWL x 5
 - Cystoscopy x 6
 - PCNL x 1
- PMH—otherwise negative

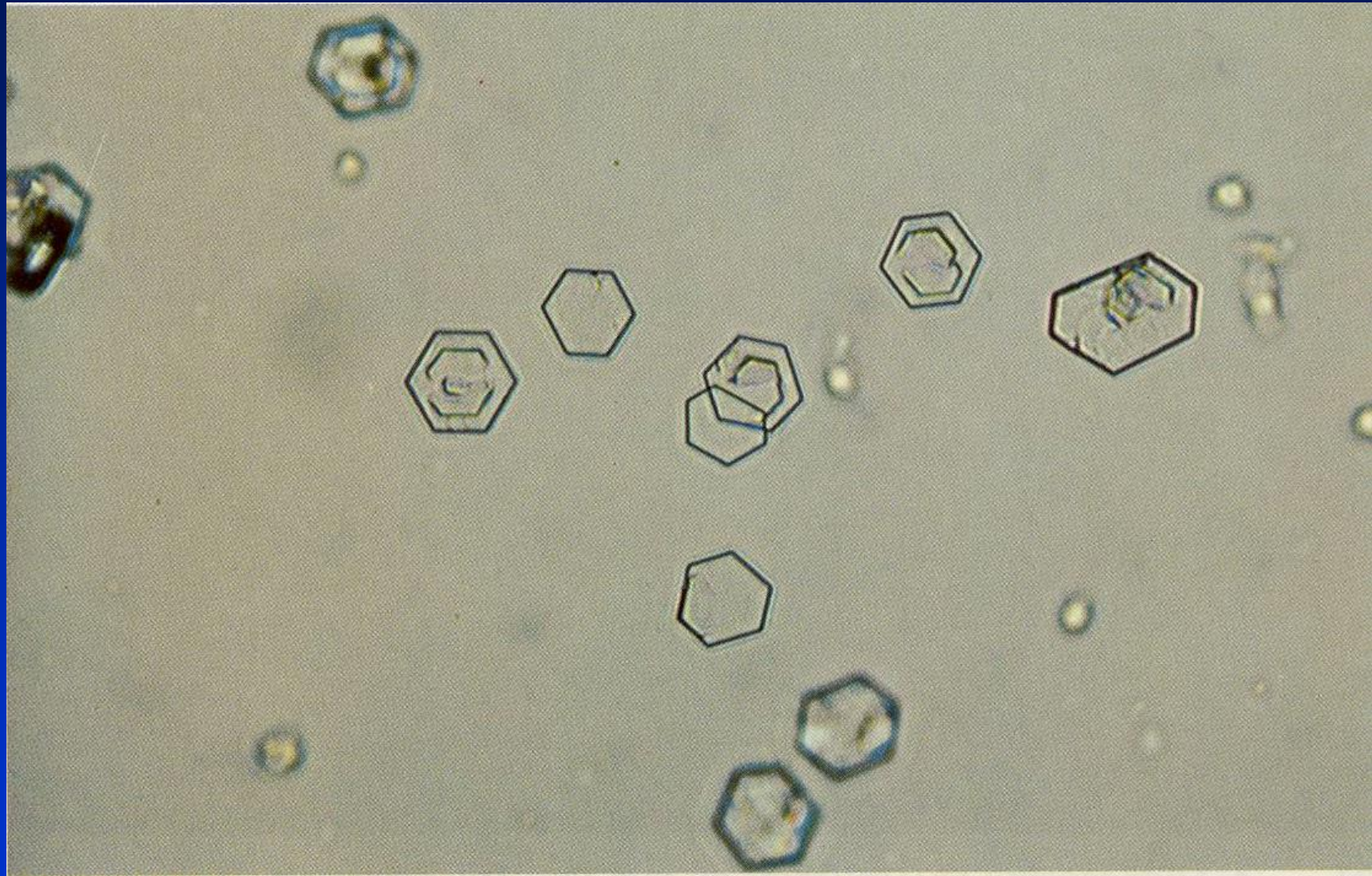
Case #2—24-hour urine

<u>TV</u>	<u>Ca</u>	<u>Ox</u>	<u>Cit</u>	<u>UA</u>	<u>Creat</u>	<u>Na</u>	<u>pH</u>
2.30	114	28	1102	396	972	168	7.30

What Is the Most Likely Stone Type?

- A. Calcium oxalate
- B. Calcium phosphate
- C. Uric acid
- D. Cystine





Answer: Cystine

- Autosomal recessive disorder
- Excessive excretion of cystine, which is poorly soluble

Medications

- Potassium citrate 20 meq BID
 - Occasionally checks urine pH
- Allergies
 - Penicillamine → rash

CT Report

Right kidney: no stones

Left kidney: 4 mm and 2 mm upper pole stones; 9 mm lower pole stone

4 mm stone at left ureterovesical junction

Case #2—24-hour urine

<u>TV</u>	<u>Ca</u>	<u>Ox</u>	<u>Cit</u>	<u>UA</u>	<u>Creat</u>	<u>Na</u>	<u>pH</u>
2.30	114	28	1102	396	972	168	7.30

Total cystine: 1877 mg/d (816 mg/L)

Treatment

- Reduce [cystine] < 250mg/L
- Increase fluid intake
 - But this alone not plausible
 - Urine output required > 7 L/d
- Tiopronin (Brand name: Thiola)
 - Typically need at least 900 mg/d (300 mg TID)
 - Extended-release generic formulations available
- Continue alkalinization aiming for pH >7.0

Case #2—6 Months Later...

- Calls with left renal colic
- Stopped medication because it clearly did not work
- Is she correct?



Shift Overlay from 60xx to 7FE0

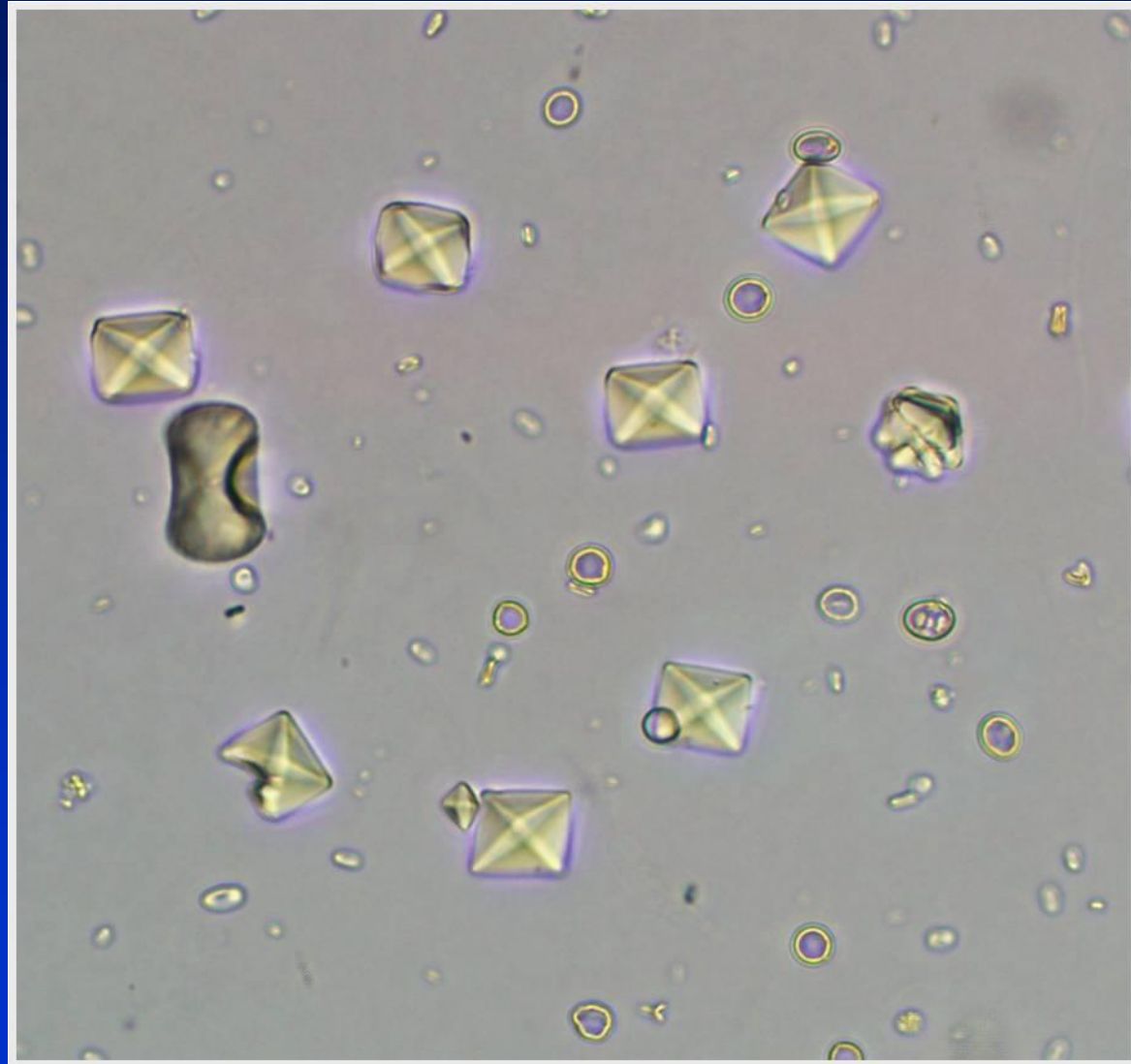


Case #3—Ms. J.B.

- 35 y.o. female nurse with recurrent stones
- Presented 5 years before with colic and bilateral renal stones
- PMH: unremarkable

What Is the Most Likely Stone Type?

- A. Calcium oxalate
- B. Calcium phosphate
- C. Uric acid
- D. Cystine



Courtesy of John Lieske

Answer:	Calcium oxalate	95%
	Calcium phosphate	5%

- Mixed calcium stones common
- Calcium oxalate most common crystal type
- Randall's plaque composed of calcium phosphate
 - Calcium oxalate grows on top of Randall's plaque

CT Report

Bilateral renal stones

- Ask radiologists to quantify number and size
- Also need impression if stone burden has changed over time

3 mm stone at left UVJ

Question: Acute Management?

- Watchful waiting
 - For how long?
 - Pain
 - Infection
 - Hydronephrosis
- Medications
 - Alpha blocker
- Cystoscopic removal
- ESWL

Urinary Risk Factors for CaOx Stones

Increased risk

Calcium

Oxalate

Decreased risk

Citrate

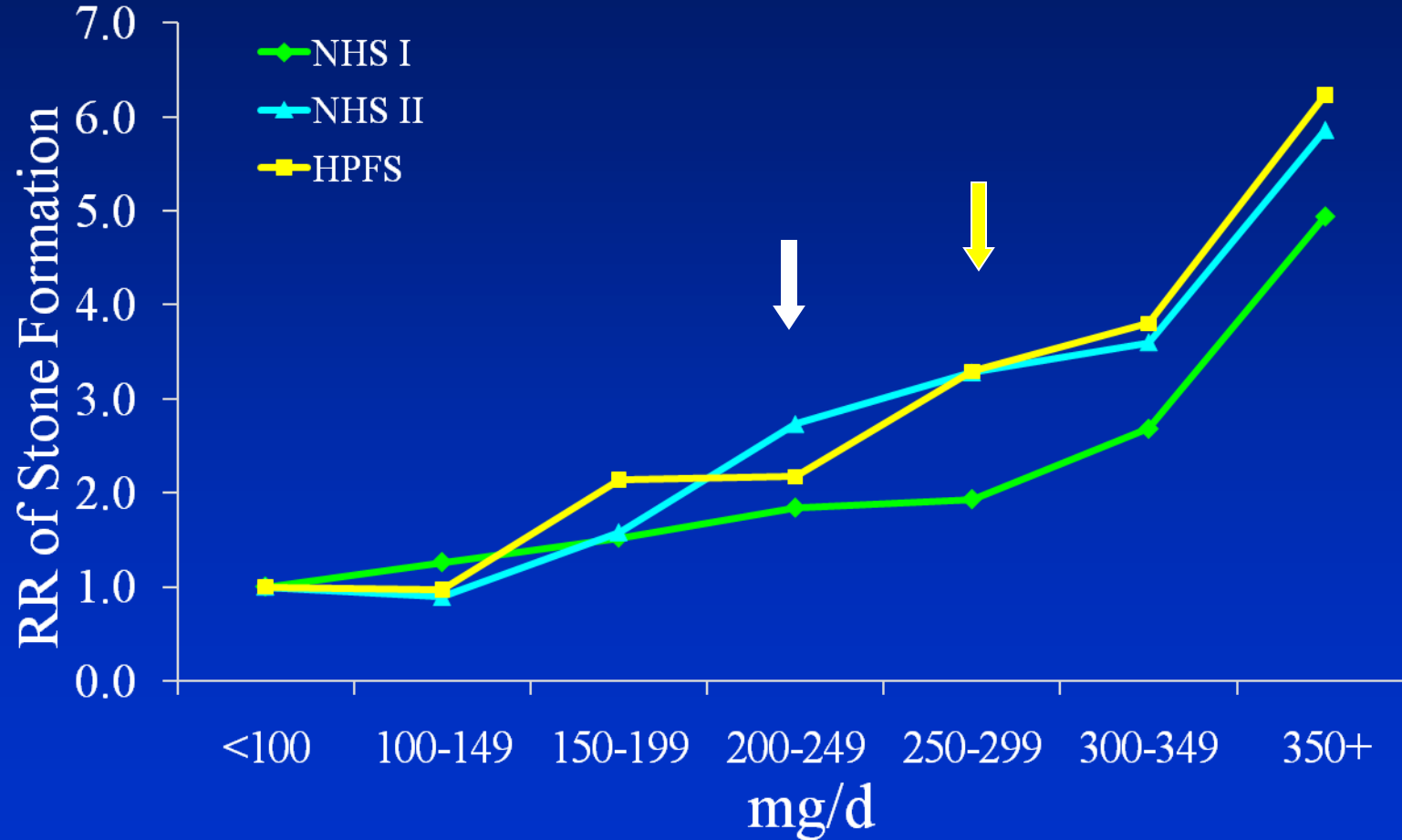
Volume

*But need to rethink our approach--these
are continuous variables, not dichotomous*

“Definitions”

- Hypercalciuria
 - Males: > 300 mg/d
 - Females: > 250 mg/d
 - Either: > 4 mg/kg/d
- Hyperoxaluria: > 45 mg/d
- Hyperuricosuria
 - Males: > 800 mg/d
 - Females: > 750 mg/d

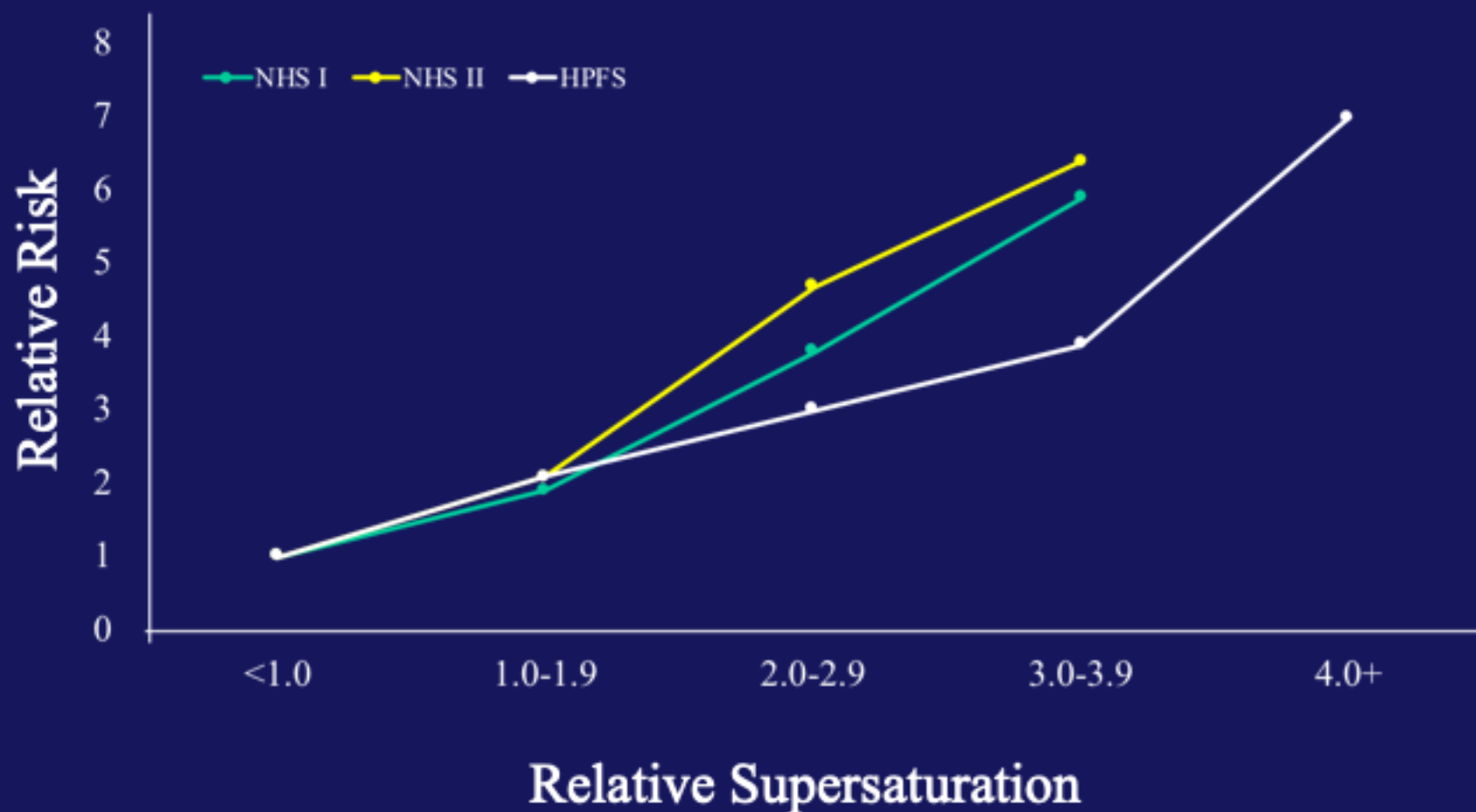
24 Hour Urine Calcium



Case #3—24-hour urine

Date	Vol 24	SS CaOx	Ca 24	Ox 24	Cit 24	SS CaP	pH	SS UA	UA 24
	Urine Volume (Preserved)	Calcium Oxalate Saturation	Calcium, Urine	Oxalate, Urine	Citrate, Urine	Calcium Phosphate Saturation	pH, 24 hr, Urine	Uric Acid Saturation	Uric Acid, Urine
06/15/2026	780	9.56	381	13	881	1.46	5.46	2.78	460
Ref. Interval	>2500	<7.50	30-200	<37	>530	<1.50	5.70-6.30	<1.00	370-750
Units	mL/24 hr		mg/24 hr	mg/24 hr	mg/24 hr				mg/24 hr

Relative Risk of Stone Former by Relative Supersaturation



Question: Treatment?

- Increase fluid intake
 - How much to prescribe?
- If TV does not increase?
- Thiazide

Table S12: Secondary End Point Analysis: Radiologic Stone Recurrence.

Group	Patients	Events	% (No. Events/ No. Patients)	Odds Ratio (95% CI)
Placebo	94	46	49%	Reference
12.5 mg HCT	98	44	45%	0.85 (0.48-1.50)
25 mg HCT	101	32	32%	0.49 (0.27-0.87)
50 mg HCT	90	31	34%	0.54 (0.29-0.98)

Question: Follow-Up?

- Repeat 24-hour urine
 - 4-6 weeks
- Adjust recommendations
- Repeat 24-hour urine
- Follow-up imaging
 - Stone growth
 - New stone formation

Advice Based on Experience

- Always measure TWO 24-hour urines at baseline
- Find out stone composition by analysis
- Repeat 24-hour urine after recommendations
- Challenging for patients to reduce sodium intake
- Helical CT is the most reliable imaging study

Advice Based on Experience

- Be careful when recommending an overly restrictive low oxalate diet
- Explain to patient that a new episode of colic does not always mean treatment failure
- The urologist is your friend

1. A 42 year old male suffered a severed spinal cord at T10. He has a long history of recurrent urinary tract infections. As part of the evaluation for abdominal pain, he had a KUB that showed a staghorn calculus in his right kidney. One of his urine infections most likely included which of the following bacteria?
 - a. E. coli
 - b. MRSA
 - c. Klebsiella pneumoniae
 - d. proteus mirabilis

(Correct answer is D)

Answer: Struvite

- Proteus is the most common urease producing bacteria
- Struvite stones only form when there is a urease producing bacterium in the upper tract.

2. A child whose parents are first cousins was found to have a kidney stone at age 7. The urinalysis showed blood and many hexagonal crystals. The most likely stone composition is:
- a. cystine
 - b. struvite
 - c. calcium oxalate
 - d. uric acid

(correct answer is A)

Answer: Cystinuria

- Cystinuria is an autosomal recessive disorder
- Excessive cystine excretion results in crystal formation
- Cystine crystals have a characteristic hexagonal shape

Additional Case

Case #4—Mr. S.L.

- 49 y.o. male accountant with h/o Crohn's disease
- S/p partial ileal resection
- Recurrent intestinal obstruction
- Presented 6 months ago with abdominal pain
- Intestinal obstruction?
- Exploratory laparotomy planned

Case #4—Mr. S.L.

- Pre-op evaluation: U/A-->100 RBC
- Underwent right hemi-colectomy
- POD #5—abdominal pain
 - due to tapering of analgesics?
- Discharged home on oxycodone
- Returned two days later to ER
- UVJ stone seen on CT

Question: Stone type?

- A. Calcium oxalate
- B. Calcium phosphate
- C. Uric acid
- D. Cystine

Calcium oxalate 100%

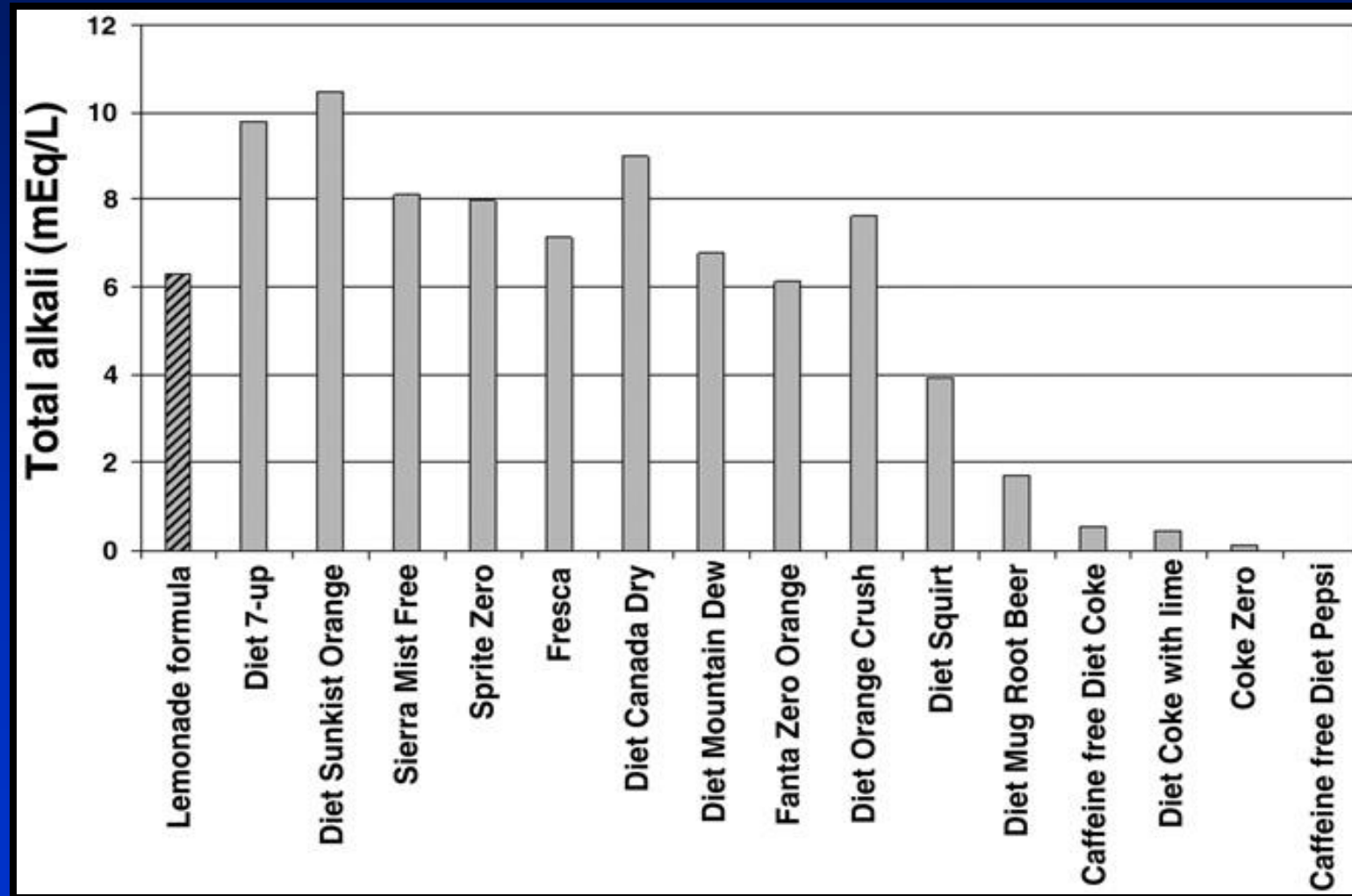
Case #4—24 hour urine

<u>TV</u>	<u>Ca</u>	<u>Ox</u>	<u>Cit</u>	<u>UA</u>	<u>Creat</u>	<u>Na</u>
1.20	62	117	18	413	1350	---
1.30	73	73	11	711	1412	---

Question: Treatment?

- Increase fluid intake
 - How much to prescribe?
- Reduce oxalate
 - Increase dietary calcium intake
- Increase citrate
 - Which formulation?

Soda, Lemonade and Citrate



TAKE HOME MESSAGES

- Kidney stones can be prevented
- Recommendations should be guided by 24-hr urine chemistries. These are continuous values and there is no absolute cutoff for “normal”.
- Obtain 24-hour urine collections to guide initial recommendations and perform follow-up collections to monitor the effectiveness of recommendations.
- Dietary and pharmacologic interventions can substantially reduce risk of stone growth and new stone formation
- Long-term follow-up will help ensure patients continue to follow recommendations.



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CLINICAL TRIALS

Clinical Trials	Change in Management	
Hydrochlorothiazide and Prevention of Kidney-Stone Recurrence (NEJM 2023;388:781-91)	No change in management	Thiazide group had lower risk of new stone formation but not for primary outcome
WHI—calcium supplements (N Engl J Med 2006; 354:669-683)	Use caution when prescribing calcium supplements in patients with a history of kidney stones	Check 24-hr urine calcium before and after starting.
Ultrasonography versus computed tomography for suspected nephrolithiasis(N Engl J Med. 2014 Sep 18;371(12):1100-10); Editorial (N Engl J Med 2014; 371:1154-1155)	Ultrasound can be considered but many patients will likely need a CT (ideally, low-dose CT to limit radiation exposure)	

